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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,752	04/05/2001	Leonard P. Guarente	0050.1491-005	1365

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225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER
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BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary

2M

Application No.

09/826,752

Applicant(s)

GUARENTE ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-18 and 20-48 is/are pending in the application.
- 4a) Of the above claim(s) 14,16-18,23,25-27 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13,15,20-22,24,28-30,35 and 37-48 is/are rejected.
- 7) ☒ Claim(s) 32-34 and 36 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Inventorship***

1. In view of the papers filed 20 October 2003, the inventorship in this nonprovisional application has been changed by the deletion of James Claus and Francesca Cole.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

### ***Claim Objections***

2. Claims 13, 15, 20-22, 24, 28-30, and 32-48 are objected to because of the following informalities: In line 1 of claims 13 and 37 the term "the" should be inserted before the term "lifespan." Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The rejection of claims 13, 15, 19-22, 24, and 28-30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 18 April 2003 is withdrawn in view of the amendment filed 20 October 2003.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 37-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a rejection for new matter. The claims are drawn to a method of identifying agents that alter the lifespan of eukaryotic cells comprising a step of exposing the cells to an agent wherein modulation of replicative capacity is due to the presence or absence of the agent as opposed to mutation induced by the agent. The specification distinguishes between agents and mutagens on page 31:

#### METHODS OF IDENTIFYING AGENTS WHICH AFFECT LIFE SPAN

The above-described methods for isolating mutant yeast cells with a longer lifespan can be employed to identify agents which alter the life span of a yeast strain. In this embodiment of the current invention, the yeast strain of interest, for which the life span is known or has been calculated, is exposed to the agent to be tested rather than subjected to a mutagen. The samples thus exposed are then examined for longer-lived colonies, using any of the methods described above. Colonies exhibiting a longer life span in the presence of the agent than in the absence of the agent are indicative of the ability of the agent to increase life span, or to postpone senescence. Agents include drugs, peptides, oligonucleotides, and genes encoding proteins that increase life span, such as genes isolated by the methods described below.

In the description of the claimed invention, the specification describes agents that are explicitly not mutagens. Newly filed claim 37 is drawn to methods of using agents that are not selected from agents that are mutagens. The applicants have attempted by argument and amendment to claim in generic claims methods of using agents that include mutagens. Because the specification excludes mutagens from the agents of the method, the newly filed claims 37-48 comprise new matter because the newly filed claims are drawn to generic agents that include mutagens. For the purpose of examination the term "agent" in the pending claims is limited as defined on page 31 of the specification to exclude mutagens.

***Claim Rejections - 35 USC § 102***

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6. The rejection of claims 13, 21, and 29 under 35 U.S.C. 102(a) as being anticipated by Fleming et al. in the Office action mailed 18 April 2003 is withdrawn in view of the amendment filed 20 October 2003 in which the claims are limited to a method in which the replicative capacity of an individual cell is determined.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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9. Claims 13, 15, 20, 21, 22, 24, 29, 35, 37-41, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fleming et al. in view of Lundblad et al. (reference AW2 in the information disclosure statement filed 04 June 2001).

The claims are drawn to a method of assaying the effect of an agent on the replicative capacity of a eukaryotic cell that is under stress. In some embodiments the replicative capacities of treated and untreated cells are determined, the cell is a yeast cell, and the stress is heat shock. In some embodiments the eukaryotic cell is genetically altered to have a different capacity for mitotic division. In some embodiments the cell is cultured for greater than the capacity of cell division of untreated cells.

Fleming et al. reviews the role of oxidative stress in aging in *Drosophila* on pages 267-269. On pages 269-272 Fleming et al. shows that production of transgenic *Drosophila* organisms comprising a bovine superoxide dismutase (SOD) gene. The bovine gene corresponds to the agent recited in the claimed invention. Fleming et al. shows in figures 1 and 2, and pages 269-272 that the transgenic *Drosophila* have an increased lifespan when placed under stress due to paraquat or 100% oxygen. Fleming et al. reviews the effect of heat shock on ageing on pages 273-277. Fleming et al. shows that heat shock induces expression of heat shock proteins, and on page 275 discusses treatment of *Drosophila* organisms with an agent consisting of canavanine to induce a heat shock response. Fleming et al. discuss the induction of SOD upon heat shock on page 276. Fleming et al. shows the effect of heat shock on survival for old and young *Drosophila* organisms in figure 5. Fleming does not show direct measurement of mitotic potential, a stress that is heat shock, or use of yeast cells.

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Lundblad et al. shows in the abstract that yeast cells mutated in the EST1 gene have a shortened lifespan. Lundblad et al. shows on page 637 the treatment of yeast cells with defective EST1 genes. Lundblad et al. shows measurement of mitotic potential in yeast strains in figures 3 and 6 and in the experimental procedures section on pages 641-642 for the purpose of determining the effect of introduced mutations on mitotic potential.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Fleming et al. by use of a stress consisting of heat shock as disclosed in Fleming, and the yeast cells and mitotic potential methods of Lundblad et al. because such a modification would allow for further insights into the role of SOD and heat shock on ageing in yeast cells.

10. Claims 13, 28, 30, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fleming et al. in view of Lundblad et al. as applied to claims 13, 15, 20, 21, 22, 24, 29, 35, 37-41, and 44 above, and further in view of Pringle (reference ARR in the information disclosure statement filed 10 January 2003) in view of Muller (reference AII in the information disclosure statement filed 10 January 2003).

The claims are drawn to a method of assaying the effect of an agent on the lifespan of a eukaryotic cell that is under stress by use of fluorescent cell surface labeling.

Fleming et al. in view of Lundblad et al. as applied to claims 13, 15, 20, 21, 22, 24, 29, 35, 37-41, and 44 above does not show use of fluorescent cell labeling.

Muller shows on page 1 that the lifespan of a yeast cell correlates with the number of bud scars on the cell. Muller shows use of bud scar counts to determine the age of yeast cells in Table 2.

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Pringle et al. shows on pages 378-380 the use of fluorescent dyes to observe bud scars.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Fleming et al. in view of Lundblad et al. as applied to claims 13, 15, 20, 21, 22, 24, 29, 35, 37-41, and 44 above by use of the fluorescent dye because Muller and Pringle et al. show that the method can be used to determine the age of yeast cells to allow for a determination of the lifespan of the observed cells.

11. Applicant's arguments filed 20 October 2003 have been fully considered but they are not persuasive. The applicants state that Fleming et al. does not show survival of cells treated with an agent but Fleming et al. does show such a survival measurement in figures 1 and 2. The applicants state that Fleming et al. does not show a correlation between stress survival and replicative capacity. Fleming et al. does show such correlations and concludes in the last sentence of the abstract:

Collectively, results from our laboratory demonstrate that oxidative damage plays a role in governing the lifespan of *Drosophila* during normal metabolism and under conditions of environmental stress.

Regarding the applicant's comments concerning Lundblad et al., Lundblad et al. uses direct measurements of mitotic potential of an individual cell to study the lifespan of yeast cells. Lundblad et al. uses this method to determine effects of chromosomal mutations on senescence. For the reasons of record it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Lundblad et al. to study the effects of stress survival on senescence in yeast cells in view of the teachings of Fleming et al. which shows the effect of stress survival on the lifespan of *Drosophila* strains.

***Allowable Subject Matter***



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12. Claims 32-34, 36, and 45-48 are not anticipated or obvious over the prior art because the prior art does not show measurement of the effect of stress survival on replicative capacity in cells treated with the agents of claims 32-34, 36, and 45-48.

13. Claims 32-34 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### *Conclusion*

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

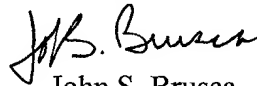
Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4028. The fax phone number for the organization where this application or proceeding is assigned is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.



John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb